
Monday, June 9

51-52

072143

Session MP1
Room 1
2:30 - 5:30 p.m.

**Mechanisms of Orthostatic
Intolerance During Real and
Simulated Microgravity**

ORTHOSTATIC TESTS AFTER 42 DAYS OF SIMULATED WEIGHTLESSNESS

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INTRODUCTION

Orthostatic intolerance remains an issue after space flights and change in autonomic cardiovascular regulation is one of the main mechanisms involved. Heart rate variability (HRV) using spectral analysis has been used as a tool for short term assessment of parasympathetic and sympathetic nervous system control of heart rate. The aim of this study was the analysis of cardiovascular responses to orthostatic tests performed before and after a prolonged 42 day (-6°) Head-Down Bed-Rest (HDBR) simulating effects of a long-duration flight.

METHODS

Seven men (28 +/-0.9 years) participated in this experiment. Blood pressure (sphygmomanometer, and continuous non-invasive finger cuff method: Finapres) and RR interval were measured at rest and during stand tests (10 min.) and Lower Body Negative Pressure (LBNP) tests (5 min. at -25, -35 and -45 mmHg) performed before (D-3) and at the end (R+1) of HDBR. We have used coarse graining spectral analysis of heart rate to extract the harmonic components for calculation of parasympathetic (PNS) and sympathetic (SNS) indicators. The integrated power in the low frequency (P_L) region (0-0.15 Hz) and in the high frequency (P_H) region (0.15-0.50 Hz) were calculated as well as total spectral power (P_T). Normalized PNS and SNS indicators were calculated as P_H/P_T and P_L/P_H respectively. Data of RR intervals and blood pressure (Finapres) were also analyzed to point up spontaneous baroreflex sequences, which reflect the heart rate responses to spontaneous variations of blood pressure and calculate spontaneous baroreflex slope (SBS).

RESULTS

4 and 1 subjects (among 7) did not complete respectively the stand and the LBNP tests at R+1. Greater heart rate increase during the stand and LBNP tests, and decrease in blood pressure during the stand tests reflecting a reduced vasomotor response, characterized the orthostatic responses at R+1 (Table I).

Table I: Heart Rate and Blood Pressure variations

STAND TEST	D-3	R+1
Heart Rate (b/min.)	+44 %	+57 %
Systolic Blood Pressure (mm Hg)	+5 %	-9 %
Mean Blood Pressure (mm Hg)	+21 %	-8 %
Diastolic Blood Pressure (mm Hg)	+18%	-10 %

Mean Heart Rate and Blood Pressure (Systolic, Mean and Diastolic) variations during STAND TESTS performed before (D-3) and after (R+1) the 42 day HDBR (n= 7). Values are expressed as percentage compared to baseline data (measured in supine position before standing up).

The main findings in HRV and SBS included after HDBR : significant reductions in RR interval and in total power suggesting a decrease in cardiovascular neurovegetative control induced by HDBR, a decrease in PNS indicator and an increase in SNS indicator, and a reduced SBS. RR interval, P_T and PNS indicator were further reduced by standing and LBNP exposure as well as SBS. The reduced PNS indicator and SBS suggest the vagal component of the cardiovascular control has been diminished.

CONCLUSION

These changes in autonomic cardiovascular control constituted important contributors to the reduced orthostatic tolerance observed in this experiment and found after space flights. The same kind of autonomic changes, but less pronounced, were already reported after HDBR of shorter duration. Several factors might play a role in cardiovascular adaptation in HDBR, in particular reduced physical activity and some autonomic changes could be opposed to those observed with training.

EFFECTS OF 12 DAYS EXPOSURE TO SIMULATED MICROGRAVITY ON CENTRAL CIRCULATORY HEMODYNAMICS IN THE RHESUS MONKEY

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INTRODUCTION

Our current understanding of cardiac and hemodynamic responses and adaptations to actual spaceflight or groundbased simulations of microgravity has been primarily limited to non-invasive measurements of heart rate, blood pressures, and echocardiography because of ethical and logistical constraints imposed on experiments in human subjects. Confirmation of microgravity effects on possible changes in cardiac function and structure as well as underlying mechanisms would be desirable. This study provided the opportunity to obtain preliminary data using a groundbased animal model to test the hypotheses that: 1) alterations in stroke volume and cardiac output during extended exposure to microgravity was associated with reduced cardiac function; and 2) that microgravity causes a change in cardiac compliance.

METHODS

Central circulatory hemodynamic responses were measured before and during 12 days of 10° head-down tilt (HDT) in 4 flight-sized juvenile rhesus monkeys who were surgically instrumented with a variety of intrathoracic catheters and blood flow sensors to assess the effects of simulated microgravity on central circulatory hemodynamics. Each subject underwent measurements of aortic and left ventricular pressures, and aortic flow before and during HDT as well as during a passive head-up postural test before and after HDT. Heart rate, stroke volume, cardiac output, and left ventricular end-diastolic pressure were measured, and dP/dt and left ventricular elastance was calculated from hemodynamic measurements. The postural test consisted of 5 min of supine baseline control followed by 5 minutes of 90° upright tilt (HUT).

RESULTS

Heart rate decreased during the initial 3 days of HDT followed by a gradual elevation and overshoot during the remainder of HDT. Stroke volume was unchanged during the initial 7 days of HDT followed by an increase during the final 5 days of HDT. As a result, cardiac output was increased during the latter phase of HDT. Left ventricular elastance was reduced throughout HDT, indicating that cardiac compliance was increased. HDT increased left ventricular +dP/dt, indicating an elevation in cardiac contractility. Heart rate during the post-HDT HUT postural test was elevated compared to pre-HDT while post-HDT cardiac output was decreased by 47% as a result of a 20% reduction in stroke volume throughout HUT.

CONCLUSION

Results from this study using an instrumented rhesus monkey suggest that exposure to a groundbased analog of microgravity may cause increased ventricular compliance and cardiac contractility. Our project revealed that an invasively-instrumented animal model should be viable for use in spaceflight cardiovascular experiments to assess potential changes in myocardial function and cardiac compliance.

INCREASED SENSITIVITY AND RESETTING OF BAROREFLEX CONTROL OF EXERCISE HEART RATE AFTER PROLONGED BED-REST

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Background

Studies during spaceflight and prolonged bed-rest simulations of spaceflight have been used to investigate basic mechanisms of orthostatic intolerance. Such studies in resting humans have shown an association between reduced sensitivity of the arterial baroreflex and orthostatic intolerance, but corresponding data from exercise have so far not been available.

Methods

We studied baroreflex control of heart rate (HR) during steady-state exercise (50 W) with superimposed sudden tilts between supine and upright posture. Seven men were studied repeatedly before and 0 (8h), 2, 4, 8, 12, and 33 days after a 42-day period of bed-rest in -6° head down tilt position. Arterial and cardiopulmonary baroreflex inputs were computed from continuous estimates of mean carotid distending pressure (CDP) and thoracic blood volume. CDP was computed from continuous, photoplethysmographic recordings of the arterial blood pressure and the pressure in a hydrostatic fluid column between the neck and the Finapres cuff. Thoracic blood volume was estimated from transthoracic electrical impedance. Cardiac output was measured with an acetylene rebreathing method in the supine and the upright positions.

The sensitivity of the carotid-cardiac and the cardiopulmonary-cardiac baroreflex was determined from HR responses to increases in CDP and central blood volume during down tilts.

Results

Our preliminary analysis indicates that both arterial and cardiopulmonary baroreflex sensitivities were increased after bed-rest and then were gradually returned to control. There was normalization of the cardiopulmonary baroreflex sensitivity 4 days but not 2 days after bed-rest and of the arterial baroreflex 33 but not 12 days after bed-rest. Eight hours after bed-rest the steady-state mean arterial pressure was approximately 20 mmHg higher than before bed-rest; this resetting was normalized 2 days later. Tilt-induced changes in central blood volume were not different after bed-rest. Steady state exercise heart rates were higher after bed-rest and had returned towards normal on day 33. Cardiac output and stroke volume were decreased, in both supine and upright position, after bed-rest and did not fully recover in 33 days. Except generally higher heart rates, no sign of orthostatic intolerance were observed during the exercise-tilt test.

Conclusion

We conclude that baroreflex control after prolonged bed-rest differs between rest and light exercise in that blood pressure resetting and increased reflex sensitivity compensate for the fall in stroke volume and thus contribute to maintaining orthostatic tolerance during exercise.

COMPLEX CARDIOVASCULAR DYNAMICS AND DECONDITIONING DURING HEAD-DOWN BED REST.

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INTRODUCTION

Chaos theory provides new tools to study cardiovascular physiology and new hypotheses about its regulation. Some authors observed an alteration in cardiovascular dynamics complexity in circumstances where orthostatic tolerance is decreased. We hypothesised that fractal and non-linear dynamics of heart rate and blood pressure variability could be changed, even at rest, during a long-term ground based simulation of weightlessness.

METHODS

Beat-by-beat series of RR-intervals and systolic blood pressure of seven resting subjects were observed before, during and after a 42 day head-down bed rest (HDBR). The fractal component of series was examined using coarse graining spectral analysis (Yamamoto & Hughson, *Physica D*. 68:250-264; 1993), while non-linear predictions (Sugihara & May, *Nature*. 344:734-741; 1990) and correlation dimensions (Grassberger & Procaccia, *Physica D*. 9:189-208; 1983) were used to evaluate non-linear dynamics of series.

RESULTS

Results showed for RR-interval a fractal change while non-linear dynamics were not changed and for blood pressure no fractal change while non-linear dynamics were slightly changed. Despite strong regulatory relationships between RR-interval and blood pressure, RR-interval fractal change had no consequence on blood pressure fractals and blood pressure non-linear dynamics changes had no consequence on RR-interval non-linear dynamics. RR-interval fractal change is also observed during parasympathetic blockade. Blood pressure non-linear dynamics changes are also observed in barodenervated dogs. The individual RR-interval non-linear predictions before HDBR indicated differences between subjects. Two subjects have high prediction coefficients, two others have low coefficients and the remaining three have intermediate coefficients. Orthostatic intolerance after HDBR was observed on four subjects who included the two subjects with low coefficients and excluded the two subjects with high coefficients.

CONCLUSION

The conclusions were 1) HDBR induced alterations in cardiovascular dynamics complexity 2) during head down bed rest, complexity alterations of RR-interval and blood pressure variability were not bounded up with one another. These alterations could be involved in orthostatic intolerance observed after HDBR. Individual results of non-linear predictions do suggest an interesting way to select non-fainter subjects. Nevertheless these preliminary results have to be confirmed.

Abstract from Simon Evetts for submission to the Universities Space Research Association, IAA Man in Space Symposium.

Evetts and Russomano (1995). The cardiovascular effects of 6 hours of head-down tilt upon athletes and non-athletes.

The cardiovascular responses of athletes and non-athletes to a simulation of microgravity comprising a 6 hour exposure to 6° head-down tilt (HDT) were investigated. Eight healthy male subjects, aged 19-33, were placed in athletic (n = 4) and non-athletic (n = 4) groups according to their directly measured maximum oxygen uptake values. The effects of the 6 hour exposure to 6° HDT were studied by recording ECG and arterial blood pressure at intervals during HDT and during 10 minutes of 70° head-up tilt before and after the HDT. Baroreceptor responsiveness was examined by recording the heart rate and blood pressure responses to Valsalva's manoeuvres (mouth pressure of 40 mmHg held for 15 seconds) performed before and after the 6 hour period of HDT, whilst the subject was horizontal and in the 70° head-up position. The increase of heart rate and the decreases of systolic and diastolic pressures produced by the head-up tilt were significantly greater ($p < 0.05$) after the 6 hour exposure to HDT than before. The athletic group were also found to have a significantly greater mean baroreflex slope when compared to that of the non-athletic group mean ($p < 0.05$). Of seven subjects who successfully completed the experimentation none fainted before HDT and two fainted after HDT. The subjects who fainted were both athletes.

The results of this investigation support the hypothesis that physical fitness and microgravity simulation both adversely affect blood pressure control mechanisms.

INDIVIDUAL SUSCEPTIBILITY TO POST-SPACEFLIGHT ORTHOSTATIC INTOLERANCE: CONTRIBUTIONS OF GENDER-RELATED AND MICROGRAVITY-RELATED FACTORS

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INTRODUCTION

The major manifestation and the most well documented (by preflight and landing day stand tests) of the cardiovascular changes associated with spaceflight is reduced orthostatic tolerance. Virtually every space traveler suffers this, although to different degrees. We now think this problem has a large autonomic component.

METHODS

In the past several years, our laboratories (*J. Appl. Physiol.* 73:664-71, 1992; *J. Appl. Physiol.* 77:1776-83, 1994; *J. Appl. Physiol.* 79:428-33, 1995; *J. Appl. Physiol.* 80:910-14, 1996; and *J. Appl. Physiol.* 81:2134-41, 1996) and others (*J. Appl. Physiol.* 81:7-18, 1996) have focused on determining the etiology of post-spaceflight orthostatic intolerance. We have recently begun to focus on the similarities and differences between short- and long-duration spaceflight and their effects on orthostatic mechanisms. Important findings have come from these studies.

RESULTS

First, there are distinct measurable individual differences in susceptibility to post-spaceflight orthostatic intolerance. Susceptible astronauts (about 25%) cannot remain standing for 10 minutes on landing day. These individuals, as a group, have different cardiovascular responses to standing, not only on landing day but also before flight, when they display lower peripheral vascular resistance and arterial pressures and higher heart rates than non-susceptible individuals. Susceptible astronauts are primarily female and primarily non-pilots.

Second, there is now clear evidence of autonomic dysfunction associated with spaceflight. During and after spaceflight, arterial baroreflex control mechanisms are attenuated, baroreflex sensitivity during Valsalva maneuvers is attenuated, and orthostatic tolerance during lower body negative pressure is reduced. On landing day, sympathetic responsiveness, measured by low frequency systolic pressure spectral power, norepinephrine release, peripheral vascular resistance, and arterial pressure, is reduced in susceptible individuals. Recent evidence from long-duration spaceflight indicates that the degree of attenuation is not greater after prolonged stays in space.

Third, all evaluations of cardiovascular changes associated with spaceflight must account for the influence of the many confounding factors which occur during spaceflight, even on dedicated life science missions. These include individual susceptibility of crew members to space motion sickness and exhaustion, sleep/wake cycles, medications, influence of conflicting research protocols, and influence of conflicting operational requirements.

CONCLUSIONS

These studies have both research and clinical applicability. We have begun to elucidate the mechanisms of post-spaceflight orthostatic intolerance. The next logical step is to explore the mechanisms of individual susceptibility, both gender-related and autonomic-related. Appropriate, individualized countermeasures may then be developed for astronauts thought to be susceptible. In addition, the mechanisms learned may be helpful to delineate mechanisms of the pathophysiology of autonomic disease.

CASSIOPEE MISSION 1996. COMPARISON OF CARDIOVASCULAR ALTERATION AFTER SHORT AND LONG-TERM SPACEFLIGHTS.

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INTRODUCTION

After a spaceflight, returning astronauts present a cardiovascular deconditioning consisting of orthostatic intolerance (OI) and a decrease in exercise capacity. Defective central integration of cardiovascular control mechanisms could be a contributory factor to OI. To assess this hypothesis we studied heart rate variability and the spontaneous baroreflex sensitivity in 14 cosmonauts before and after several MIR missions (14 days - 6 months).

METHODS

We studied two different spaceflight durations: from 14 to 30 days (4 cosmonauts) and from 4 to 6 months (10 cosmonauts). Stand tests were performed within 60 and 30 days before launch, the first day of landing (L1), the second day (L2) and the fifth or sixth day (L5/6). Heart rate variability was studied at supine rest using coarse graining spectral analysis. This method provided indicators of the sympathetic and parasympathetic nervous influence to the heart (SNS and PNS respectively). Spontaneous baroreflex slope was obtained by continuous monitoring of arterial blood pressure and RR-interval. This method estimates the spontaneous baroreflex sensitivity.

RESULTS

In our study, on L1, 4 of 14 cosmonauts did not complete the stand test because of presyncopal symptoms. Pre and postflight supine overall variability and spontaneous baroreflex results were similar after short and long-term spaceflights. After flight, in all cosmonauts, we observed a decrease of overall variability with a significant decrease of PNS indicator associated with an increase of SNS indicator. Both PNS and SNS indicators returned to preflight values on L5/6, whereas overall variability was still altered. Moreover, a significant decrease of spontaneous baroreflex sensitivity was observed on L1. Systolic blood pressure increased on L1 and returned to preflight values, while resting RR-interval was decreased from L1 to L5/6. However, for Cassiopée mission (1 woman during 17 days) we did not observe any modification during and after flight.

CONCLUSION

These findings suggest that cardiovascular alteration develops early (before 14 days) during spaceflight and do not progress until 6 months. In addition, the incidence of OI seems to have no relation with the spaceflight duration.

CEREBRAL and FEMORAL FLOW RESPONSE to LBNP during 6 MONTH MIR-SPACEFLIGHTS (93-95).

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INTRODUCTION: The objective of this study was to assess the heart rate and the peripheral arterial response to LBNP, in order to evaluate the orthostatic tolerance of 6 cosmonauts during 6 month Mir spaceflights.

METHOD: During LBNP the cerebral and femoral flows were monitored by using Doppler probes fixed on the skin, blood pressure (arm cuff) and ECG were also measured. The calf volume changes were assessed by plethysmography. The following parameters were calculated beat by beat: cerebral flow volume (Qc) and vascular resistance (Rc) changes (3) (in % of the pre LBNP value), femoral flow volume (Qf) and vascular resistance (Rf)(1,2), cerebral to femoral flow volume ratio (Qc/Qf)(4), heart rate (HR), mean blood pressure (MAP) and calf circumference (Calf C). The LBNP test consisted in 2 steps of 10mn long at -25mmHg and -45mmHg. Seven cosmonauts were submitted to LBNP preflight (-30d), inflight (at 1month, 3 to 4m, and 5.5 m), and postflight at +7 days. Data are presented as mean values on the 6 cosmonauts.

RESULTS: The HR increased (+20% +/-7 at -25mmHg; +40% +/-8 at -45mmHg) and MAP decreased (-5% +/-3 at -25mmHg; -8% +/-3 at -45mmHg). Rc decreased by 4% +/-4 at -25mmHg; 8% +/-5 at -45mmHg pre in and postflight. Qc decreased (3% +/-3 at -25mmHg; 8% +/-3 at -45mmHg) pre in and postflight. No significant difference was found for HR, MAP, Rc and Qc pre in and postflight. Rf increased significantly less inflight at 1m, 3-4m, and 5.5m, and postflight (+16% +/-3 at -25mmHg; +18% +/-5 at -45mmHg) than preflight (+40% +/-5 at -25mmHg p<0.01; +60% +/-5 at -45mmHg p<0.01). Qf decreased less inflight and postflight (-19% +/-7 at -25mmHg; -24% +/-3 at -45mmHg) than preflight (+32% +/-7 at -25mmHg p<0.05; -43% +/-5 p<0.05). The Qc/Qf flow volume ratio increased less inflight and postflight (+21% +/-7 at -25mmHg; +23% +/-6 at -45mmHg) than preflight (+46% +/-7 at -25mmHg p<0.05; +75% +/-6 at -45mmHg p<0.01). The calf circumference increased less at -45mmHg inflight (1m and 5.5m) and postflight (6% +/-1.5) than preflight (9% +/-1 p<0.05). (Fig 1 to 6)

CONCLUSION: The cerebral flow response remained adequate at any time during the flight or postflight, and comparable to preflight, which is in favor of the conservation of an efficient cerebral vascular regulation even after 6 months in Og. A significant lack of lower limb arterial resistance increase was observed in all cosmonaut inflight and postflight. This abnormal response may be in relation with a reduced vasoreactivity of the lower limb arterial bed, a reduction of the venous tone and muscle pressure, but also with an alteration of the baroreflex. As a consequence the cerebral to femoral flow volume ratio increased less inflight and postflight. This parameter confirmed a less efficient flow redistribution toward the brain although there was no significant reduction of the cerebral flow volume. The reduced calf volume increase was not in agreement with the increased venous distensibility found after head down tilts. This apparent contradiction may be due to the fact that in head down tilt the leg veins are empty, whereas inflight they are not empty and thus cannot expand during LBNP as much as after head down tilt. The amplitude of the vascular response to LBNP remained similarly altered throughout the flight which leads to suspect that the orthostatic intolerance develops very early inflight but remains stable at least for 6 months. During inflight LBNP no abnormal response in BP or HR was found leading to suspect that orthostatic intolerance will not exist postflight. Nevertheless all cosmonauts presented sign of orthostatic intolerance postflight which demonstrates the high sensitivity of the lower limb vascular resistance and the cerebral to femoral flow ratio as measured by Doppler ultrasound for the diagnosis of reduced orthostatic tolerance. These results confirm that during long term flights the cerebral hemodynamic response to fluid shift toward the legs (as induced by LBNP) is well maintained, however the lower limb arterial and venous reactivity are severely affected. Reliable hemodynamic indicators of inflight orthostatic intolerance (lower limb vascular resistance, flow redistribution ratio) have been successfully tested, and could be used for monitoring the efficiency of the countermeasures designed to improve orthostatic tolerance inflight (ie intensive LBNP..). Nevertheless only some components of the cardiovascular disadaptation were identified. The volemia was only moderately reduced, the hormonal system and the baro-reflex were not investigated during these flights. (Work supported by CNES grants)

References: 1 - Arbeille. Ph et al. High vascular resistance quantification by Doppler method. Ultrasound Med Biol. vol 21; n°3; p 10-18. 1995

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- 4 - Ph. Arbeille, Achaibou.F, G.Fomina, et al. Regional Blood Flow in Microgravity: Adaptation and Deconditioning. Medicine & Science in Sport & Exercise; vol 28; n°10: p 14-25. 1996.

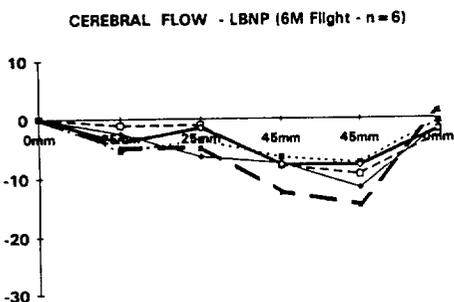


Fig 1: Middle cerebral mean flow velocity (Qc) changes in % of pre LBNP value. Changes in Qc pre, in, and post flight were not significantly different.

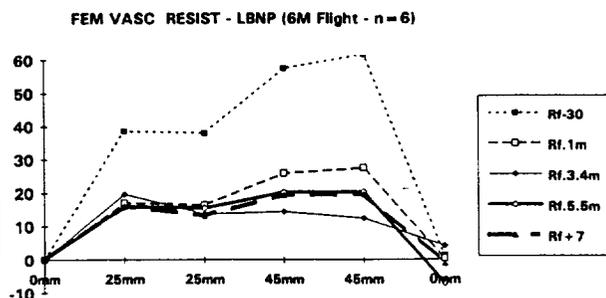


Fig 4: Lower limb vascular resistance (Rf) changes in % of the pre LBNP value. Rf increased less inflight and postflight than preflight ($p < 0.01$).

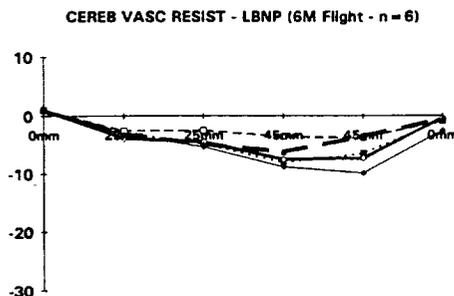


Fig 2: Middle cerebral vascular resistance (Rc) changes in % of pre LBNP value. Changes in Rc pre, in, and post flight were not significantly different.

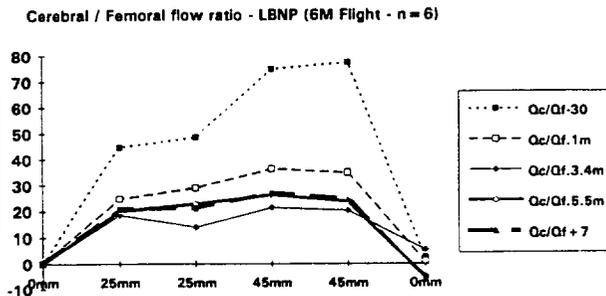


Fig 5: Cerebral to femoral flow ratio changes ($Qc/Qf = \text{Cerebral mean flow velocity} / \text{Femoral mean flow}$), in % of pre LBNP value. Qc/Qf increased less inflight and postflight than preflight ($p < 0.01$).

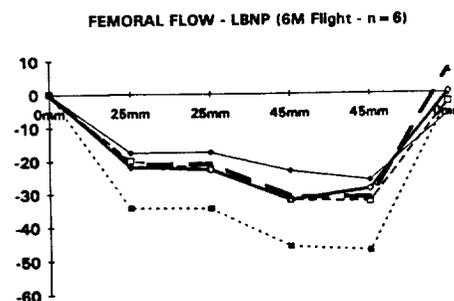


Fig 3: Femoral mean flow (Qf), changes in % of the pre LBNP value. Reduction of Qf was lower inflight and postflight ($p < 0.05$).

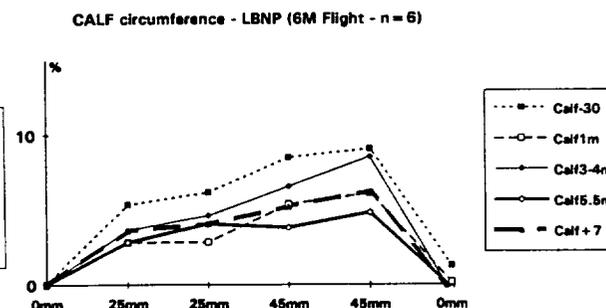


Fig 6: Calf cross section changes measured by ultrasound Plethysmography. (Calf), in % of the pre LBNP value. Calf section increased less inflight and postflight than preflight ($p < 0.05$).

CEREBROVASCULAR CHANGES DUE TO SPACEFLIGHT AND POSTFLIGHT PRESYNCOPE.

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INTRODUCTION

Virtually every astronaut returning from space exhibits symptoms of presyncope. Recently we reported that this may be due to centrally mediated hypoadrenergic responsiveness (Fritsch-Yelle *et al.* *J. Appl. Physiol.* 81(5):2134-2141, 1996). In this paper we investigate the cerebrovascular changes due to spaceflight and the interaction of the cardiovascular and cerebrovascular systems.

METHODS

Forty astronauts were studied 30 and 10 days before launch, on landing day (1-2 h after landing), and 3 days after landing, on shuttle missions lasting 8-16 days. Due to difficulty in collection and analysis of cerebral blood flow only 32 astronauts, whose mean age was 39.8±5.2 yr, had sufficient data for analysis. Middle cerebral artery flow velocity (MFV), measured with a 2-MHZ pulsed transcranial Doppler ultrasound, and blood pressure, measured using the non-invasive Finapres, were recorded on digital tape and the final 256 beats in the supine and stand position were analysed off-line. Mean arterial blood pressure was adjusted to brain level (MAP_{brain}). After ~30 min. supine, subjects were assisted to the stand position and remained unassisted in the standing position for 10 min. Subjects who became presyncopal (PSL) were returned to a supine position. Subjects were grouped based on landing day presyncope. A repeated measures analysis of variance was used. Student's *t*-tests were performed to document differences when there were significant main effects.

Coarse-graining spectral analysis, CGSA, (Yamamoto & Hughson, *Physica D* 68:250-264, 1993) was used to characterize the harmonic and fractal power. Harmonic power was divided into low (P_{LO}) and high (P_{Hl}) frequency components. The fractal power was used to determine the complexity of blood pressure and cerebral blood flow regulation with the fractal spectral exponent, β . Complexity is thought to relate to the number of mechanisms interacting to produce the measured physiological signal. High and low degrees of regulatory complexity are indicated by values of β close to 1.0 and 2.0, respectively. Cross-spectral analysis was used to determine the transfer magnitude, TM, between MAP_{brain} and MFV (Blaber *et al.* *FASEB J.* 10(3):A587, 1996). We averaged the TM over the low frequency range (0.03 to 0.14 Hz) where the squared coherence (Coh²) function was greater than 0.5. The TM serves as an indicator of what magnitude of change in MFV is due to a change in MAP_{brain}. To determine the gain, TM (cm•s⁻¹•mmHg⁻¹) was normalized, by the average cerebrovascular resistance (CVR = MAP_{brain}/MFV) over the 256 beats, and converted to dB (Gain = 20•log[TM•CVR]). Gain therefore reflects the dynamic response of MFV to MAP_{brain} along with the CVR about which the variation occurs. If autoregulation serves to regulate the effect of changing MAP_{brain} on MFV, increased gain would indicate reduced effectiveness.

RESULTS

Eight of the astronauts were PSL on landing day. MAP_{brain} decreased significantly upon standing on all three measurement days in both the PSL and nonPSL group. The PSL group had consistently lower supine MAP_{brain}. On landing day nonPSL supine MAP_{brain} was greater than it was preflight (Table 1). CGSA and Cross-spectral gain data are shown in Table 1. CGSA of the input to autoregulation (MAP_{brain}) revealed interesting differences between nonPSL and PSL astronauts. In the nonPSL astronauts P_{LO} increased from supine to stand preflight (p<0.001) and after landing (p=0.01). The PSL group showed no changes with stand pre and postflight, with landing day P_{LO} less than the nonPSL group (p=0.046). MAP_{brain}- β decreased from supine to stand in the nonPSL group preflight (p=0.011) but not postflight and was lower during postflight stand than preflight (p=0.015). The changes in MFV P_{LO} reflected those in MAP_{brain}. MFV- β did not change from supine to stand preflight in both groups, however, supine MFV- β was increased in the nonPSL immediately on landing and also decreased significantly upon standing (p=0.027). The PSL group had no significant changes in MFV- β pre to postflight or from supine to stand.

Although the trends with P_{LO} were similar between *MAP_{brain}* and MFV the effect of autoregulation can be determined by the degree to which variations in *MAP_{brain}* are translated into variations in MFV. The standing gain increased ($p=0.047$), from pre to postflight in the PSL, but not the nonPSL group. The nonPSL group showed significant decreased gain from supine to standing on all three days of measurement, whereas the PSL group showed no decrease.

Table 1: CGSA of, and Cross-spectral analysis between, *MAP_{brain}* and MFV of nonPSL (n=24) and PSL (n=8) astronauts.

		Preflight		Landing		Postflight	
		supine	stand	supine	stand	supine	stand
CGSA of <i>MAP_{brain}</i>							
nonPSL	MAP	80.8±1.8	63.3±2.4†	89.3±2.7‡	66.7±3.2†	85.8±2.3	62.2±3.5†
	P_{LO}	0.94±0.23	2.87±0.41†	1.47±0.37	3.63±0.60†	1.13±0.28	1.89±0.29
	β	1.73±0.09	1.38±0.10†	1.67±0.09	1.70±0.07‡	1.64±0.08	1.63±0.09
PSL	MAP	74.5±3.4	59.2±4.4†	75.9±5.3 [#]	61.7±5.5†	80.5±6.1	71.7±5.6†
	P_{LO}	1.42±0.75	2.00±0.58	2.07±1.38	1.65±0.34 [#]	0.77±0.17	2.21±0.89
	β	1.54±0.16	1.44±0.11	1.70±0.21	1.76±0.21	1.62±0.26	1.51±0.16
CGSA-MFV							
nonPSL	MFV	53.4±5.5	43.1±2.1†	47.6±2.3	39.7±1.6	50.6±3.0	46.1±3.0
	P_{LO}	0.34±0.07	0.99±0.20†	0.81±0.20	1.16±0.26	0.86±0.27‡	0.83±0.14
	β	1.42±0.07	1.22±0.11	1.61±0.11	1.24±0.08†	1.39±0.67	1.26±0.08
PSL	MFV	58.9±5.7	51.2±2.5†	52.4±4.7	40.0±2.9	63.3±7.2	57.0±6.8
	P_{LO}	0.46±0.12	0.68±0.14	1.83±1.22	0.49±0.99	0.93±0.47	1.01±0.28
	β	1.27±0.16	1.16±0.13	1.39±0.25	1.38±0.09	1.49±0.11	1.19±0.14
Cross-spectral analysis							
nonPSL	Gain	2.90±0.68	0.26±0.62†	2.20±0.68	0.32±0.47†	2.78±0.55	-0.25±0.70†
PSL	Gain	1.84±1.39	-1.04±1.07	2.23±1.06	2.40±2.20	2.09±1.65	2.29±1.35‡

Values are means±SE; n, no of subjects; all $p<0.05$. †, significantly different from supine; ‡, significantly different from Preflight; [#], significantly different from nonPSL.

Units: *MAP_{brain}*- P_{LO} (mmHg²•Hz⁻¹); MFV- P_{LO} (cm²•s²•Hz⁻¹); Gain (dB).

CONCLUSIONS

The intergroup differences before flight suggest that there is a subset of the normal population who have orthostatic responses within normal ranges before flight but who are predisposed to postflight presyncope (Fritsch-Yelle *et al.* *J. Appl. Physiol.* 81(5)2134-2141, 1996). This group clearly had an impaired preflight sympathetic response to tilt as indicated by an unchanging *MAP_{brain}* and MFV P_{LO} upon standing. Upon landing this value was significantly lower than the nonPSL group. As well, the standing cerebrovascular gain was higher 3 days after landing. Although the PSL group had no changes in MFV complexity, the values were consistently high (β close to 1.0), this coupled with the lower *MAP_{brain}* and slightly higher MFV than the nonPSL group pre and postflight would suggest that the autoregulatory system in the PSL group was on the leftward side of the curve, closer to maximum capacity. Cerebrovascular gain was not affected by spaceflight in the nonPSL group. NonPSL *MAP_{brain}* and MFV complexity in the supine position were reduced on landing day. *MAP_{brain}* complexity failed to change with stand, however MFV complexity increased. These data suggest that in spaceflight the number of regulatory inputs used by the body to regulate blood pressure and cerebral blood flow is reduced. Cerebral autoregulation may be adversely affected on return from spaceflight in the PSL but not the nonPSL astronauts.